Research Article

Investigating the Relationship Between Clinical Characteristics of 2019 Novel Coronavirus Pneumonia Cases (COVID-19) Before Intubation and Treatment Outcome After 14 Days in Imam Khomeini Hospital Complex, Tehran, Iran: Descriptive-Analytic Study

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Abstract

In December 2019, a new pathogen, HCoV, or New Corona Virus 2019 (2019-nCoV), was recognized in Wuhan, China, causing a pandemic. COVID-19 has a wide range of clinical severity. Approximately 3.2% of patients with some periods of the disease require intubation and invasive ventilation.

Methods: This was a descriptive-analytical study and conducted in the spring of 1399 in Imam Khomeini Hospital. Patients with COVID-19 who required endotracheal intubation were identified and their clinical symptoms and laboratory parameters were recorded. SPSS23 software was used for statistical analysis.

Results: 120 COVID-19 patients with different conditions were evaluated. The mean age was 55±14. All patients had some degree of acidosis before intubation. Lymphopenia was a common finding among patients before intubation, but thrombocytopenia and thrombocytosis were very rare. The highest mortality was observed in blood group A, but blood group O had the highest discharge from ICU. SOFA and APACHE scores were significantly associated with treatment outcome in all three groups of patients. Discussion: Although all laboratory parameters and patients symptoms can affect the treatment outcome, it was found that WBC and absolute lymphocyte count, BUN, SOFA and APACHE scores, inflammatory index ratio CRP/LDH% CRP/ESR% and ESR/LDH%, arterial blood gas indices, pulse rate, and patient temperature before intubation are among the parameters that can affect the patient's 14-day prognosis.

Conclusion: Except for the mentioned items, CRP/LDH% ratio seems to be a good indicator for checking the prognosis of discharge or death of patients within 14 days, However, CRP/ESR% and ESR/LDH% are appropriate criteria for determining the prognosis for discharge or stay in the ICU for more than 14 days.

Keywords: COVID-19, Intubation, ICU, CRP, LDH, Invasive ventilation.

Introduction

Human coronavirus is one of the main pathogens of respiratory infections. These two highly pathogenic viruses, SARS-CoV and MERS-CoV, cause severe respiratory syndrome in humans and four other human coronaviruses (HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1) cause mild upper respiratory tract disease. The major SARS-CoV outbreak, which affected 8,422 patients between 2002 and 2003, spread to 29 countries worldwide (18,19). Human coronaviruses (HCoVs) have long been considered trivial pathogens and cause "colds" in healthy people. In December 2019, a new HCoV pathogen, or 2019 novel-coronavirus (2019-nCoV), was identified in Wuhan, China, causing serious illness and death. The extent and ultimate impact of this outbreak are currently unclear as the situation is rapidly evolving [1]. The most common and severe complication in patients with COVID-19 is acute hypoxemia or acute respiratory syndrome (ARDS), which requires oxygen therapy and ventilation [3]. They had aggressive intubation and ventilation [3,4]. Approximately 3.2% of patients with COVID-19 require intubation and invasive ventilation during some periods of the disease [2] 19.

Confirmation or suspicion could be done. Some of these surgeries were performed under general anesthesia with endotracheal intubation. The intubation and ventilation of patients with COVID-19 who are highly sensitive or require urgent surgical intervention pose some unique challenges for health care providers [3-4]. COVID-19 has a wide range of clinical severity, ranging from asymptomatic to critically ill and ultimately death [5,6,7]. Which may be necessary in patients with cardiopulmonary arrest or jeopardized airway. In patients with acute COVID-19-induced acute respiratory hypoxemia, it can be challenging to decide whether to continue intubation and invasive ventilation [2,8]. For patients with improvement in respiratory distress, tachypnea (respiration rate greater than 30 beats per minute), and poor oxygenation (Pao2 versus Fio2 less than 150mm Hg) after 2 hours of high-flow oxygen therapy or non-invasive ventilation takes [9]. Most people infected with the COVID-19 virus have a mild illness and are recovering, according to the World Health Organization.

Approximately 80 laboratory-confirmed patients with mild adjustment, including non-pneumonia and those with pneumonia, will have 13.8 severe illnesses (shortness of breath, respiratory rate /30 per minute, blood oxygen saturation 93, PaO2 to FiO2 ratio less than 300, and/or lung infiltration>50 from the lung background in 24-48 hours) and 6.1 are highly critical (respiratory failure, septic shock, and/or dysfunction / organ failure) [27]. In a descriptive study in Wuhan, China, which examined the symptoms of 99 patients with COVID-19, many patients with functional organ damage, including (17%) with ARDS (8%) with acute respiratory injury, 3% had acute kidney damage, 4% had septic shock and 1%

had ventilator-induced pneumonia [10]. In terms of laboratory tests, the absolute number of lymphocytes is reduced in most patients. This result suggests that 2019-nCoV may act primarily on lymphocytes, especially T lymphocytes, such as SARS-CoV. Virus particles spread through the respiratory mucosa and infect other cells, cytokine storm Induce in the body, trigger a series of immune responses, and alter peripheral white blood cells and immune cells such as lymphocytes.

Some patients with ARDS and septic shock progress rapidly, eventually leading to failure. Multiple limbs were associated. Therefore, early detection and timely treatment of important cases is of particular importance. Absolute low lymphocyte counts can be used as a reference in the diagnosis of new coronavirus infections in the clinic [10]. Some studies suggest that A significant reduction in the total number of lymphocytes indicates that the coronavirus consumes (depletes) many immune cells and inhibits the function of the body's cellular immune system. T lymphocyte damage may be an important factor in exacerbating patients [11-15]. ARDS was present in 20 of 138 patients and in 61 of 36 patients admitted to the Intensive Care Unit (ICU) at Zhongnan Hospital in Wuhan [4]. Dysfunction, injury, or organ failure, except for the lungs, is common. Heart damage occurred in 23, liver damage in 29 and acute kidney damage in 29 critically ill patients [3]. Neurological disorders occur in more than one-third of patients with advanced COVID-19.7 [8]. Decreased susceptibility of women to viral infections can be attributed to protection against the X chromosome and sex hormones, which play an important role in innate immunity and adaptation [16-19].

Like MERS-CoV viruses, almost half of the patients infected with 2019-nCoV had chronic underlying disease: mainly cardiovascular disease and diabetes [14]. Mortality SARS- CoV more than 10 and MERS-CoV with more than 35 have been reported [20,21]. Regarding the mortality rate of patients with 2019-nCoV, 11% has been reported in two studies [6,7]. Additional deaths may occur in people who are still hospitalized. Another study found that ICU patient mortality was improved by 20.5%, as well as 21.1% of ICU non-hospitalized patients [31]. The laboratory results of a meta-analysis showed that lymphocytopenia (64.5), increased CRP (44.3), increased LDH (28.3) and leukocytopenia (29.4) were more common, and in general, all of them were compatible with respiratory virus infection [22]. Studies have also shown that the level of inflammatory cytokines may be associated with disease severity, which is expected to be an indicator of disease severity [6,23,24]. The SOFA score is a good diagnostic marker for sepsis and septic shock and indicates the status and degree of dysfunction [25,26].

A retrospective cohort study of several risk factors for adult death in Wuhan with COVID-19 In particular, older age,

d-dimer levels above 1μg/ml, and higher SOFA score at baseline were associated with a higher chance of death in hospital [24]. Thrombocytopenia in patients with COVID-19 has been observed and may be multifactorial [27]. In SARS, it has been suggested that a combination of viral infection and mechanical ventilation may lead to platelet activation, accumulation damage, and thrombosis in the lungs, leading to high platelet intake. As the lung may be a site of platelet diffusion from fully mature megakaryocytes, intermittent morphological depletion in the pulmonary capillary substrate may lead to platelet failure [28]. Coronaviruses may also directly infect bone marrow elements because of abnormal hematopoiesis [29], triggering an autoimmune response against blood cells. It has also been suggested that moderate-to-reduced DIC may produce lower platelet counts in SARS [28]. A study to evaluate lactate dehydrogenase as a risk factor for patients with coronavirus found that LDH was positively correlated with both APACHE II and SOFA scores, as well as PSI and CT. In addition, as a protective agent the lymphocyte count was less than 1.045x109/liter.

Good accuracy in identifying severe patients, maximum specificity (91/30) and sensitivity (24/95) showed. In addition, LDH was positively correlated with CRP, AST, BNP and cTnI, while it was negatively correlated with lymphocyte cells and its subsets including CD3+, CD4+ and CD8+ T cells (P<0.01). The study also found that LDH is a powerful predictor of early detection of lung damage and severe cases of COVID-19. Importantly, the number of lymphocytes, especially CD3+, CD4+ and CD8+ T cells in the peripheral blood of COVID-19 patients, which was related to serum LDH, was dynamically correlated with disease severity [30]. With higher APACHE II and SOFA scores, high PCT levels, excessive fluid volume, and delayed corticosteroid use may increase the risk of death [31]. The results of a study in China showed that blood type A was more dangerous. Achieving COVID-19 was associated with a lower risk of infection compared with non-A blood groups compared with non-A blood groups. This is the first observation of the association between ABO blood type and COVID-19, although more research is needed to confirm this [32]. Preliminary studies on the effect of BCG vaccination suggest that BCG vaccination is the number of reported COVID cases. Reduces-19 in a country.

The combination of reduced morbidity and mortality makes BCG vaccination a potential new tool in the fight against COVID-19 [33,34]. Given that there is currently no definitive cure for coronavirus-19 pneumonia, and supportive therapies such as oxygen therapy, mechanical ventilation, and nutritional support are the basis of these patients' treatment process, and given that Many of the treatments offered are clinical trials and research. Knowing what the patient is at and what the patient's prognosis may be of great help to physicians and researchers in choosing different treatments and clinical strategies. Therefore, according to the research records in the field of clinical signs and laboratory parameters of patients with COVID-19, as well as mechanical ventilation and endotracheal intubation, it is necessary to study the relationship between clinical signs and laboratory parameters of patients before intubation and Outcome/outcome of their treatment.

Methods and Materials

This is a descriptive-analytical study that was conducted in the spring of 1399 (April to June 2020) in Imam Khomeini Hospital. This article has an ethics code number IR.TUMS.VCR.REC.1399.389. Patients with Covid-19 who required endotracheal intubation were identified and their clinical signs and laboratory parameters were recorded. These include: vital signs (SPO2,HR,BP,T), inflammatory factors (CRP,LDH,PCT,ESR), Complete Cell Count (CBC), Arterial Blood Gas Factors (ABG or VBG), Liver Function Test (ALT, AST), Electrolytes (Na,K,Ca) and Blood Urea Nitrogen and Creatinine (BUN, Cr) were recorded. The patient's clinical condition including underlying disease (such as diabetes, hypertension, etc.) and Either co-morbidity (such as acute renal failure, or ventilator-induced pneumonia) was extracted from the patient's record. APACHE 2 and SOFA scores were also calculated. After intubation, patients were followed for 14 days to determine the outcome of their treatment. Patients were divided into three groups based on the outcome of treatment: group 1 patients who recovered/discharged within 14 days, group 2 patients who remained in the ICU for more than 14 days, and group 3 patients who died within 14 days. After collecting data, data were analyzed by SPSS-23 statistical software. Descriptive statistics including mean and standard deviation were used. Also, inferential statistics including one-way variance (ANOVA) were used. To analyze the qualitative variables, Phi and Cramer correlation coefficient analysis was used.

Results

In this study, 120 patients were evaluated. The demographic information of the patients is given in Table 1. Underlying diseases were extracted from the records of 25% of patients with cardiovascular and cerebral diseases (such as hypertension), 16.7% with diseases of the endocrine system (such as diabetes) and 14.2% with respiratory diseases (such as asthma or COPD). In general, patients were divided into 14-day survival: survival and non-survival. Therefore, according to the survival (50.8%) of 61 patients and death (49.2%) of 59 patients, the mortality rate was 49.2%. 22.5% of patients showed several associated comorbidity conditions within 14 days (such as acute renal failure with pneumonia). Acute respiratory failure and respiratory distress syndrome were also observed in 19.2% of patients. 10% of patients experienced acute lung or kidney injury.

Table 2 To examine the correlation of qualitative variables, Phi and Cramer correlation analysis were used. Based on Phi and Kramer correlation analysis, a significant correlation was found between comorbid disease and patient outcome (P-Value=0.00),

blood group and outcome treatment (P-Value=0.01). However, no statistically significant correlation was found between the underlying disease and therapeutic outcome (P-Value=0.19) [Table 3-5]. 31 patients (25.8%) had no accompanying condition, 27 patients (22.5%) had more than 1 accompanying condition, 23 patients (19.16%) had respiratory distress syndrome and 12 patients (10%) had acute renal failure or suffered from acute respiratory failure. The frequency of patients' blood groups was A (30%), B (25.8%), O (25%) and AB (19.16%), respectively. The highest mortality was observed in blood group A, blood group O had the highest discharge from ICU and most patients who were in ICU for more than 14 days had blood groups AB and O. Cardiovascular diseases, endocrine diseases and respiratory diseases were the most common underlying diseases, respectively.

Table 1: Demographic information

Percent	Frequency	
Sex		
52.50%	63	Male
47.50%	57	Female
BCG Vaccination		
65%	78	Yes
35%	42	No
Smoking		
30.80%	37	Yes
69.20%	83	No
Blood Group		
30%	36	A
25.80%	31	B
19.20%	23	AB
25%	30	O
Underlying Diseases		
10%	12	Any
25%	30	Cerebrovascular disease
5.80%	7	Tumors/malignancy
16.70%	20	Endocrine disease
13.30%	16	Digestive disuse
4.20%	5	Nerve system disease
14.20%	17	Respiratory disease
1.70%	2	Renal disease
9.20%	11	None
Outcome		
49.20%	59	Died within 14 days
21.70%	26	Discharged within 14 days
29.20%	35	Remained in the ICU for more than 14 days

Table 2: Laboratory results of patients

	N	Minimum	Maximum	Mean	Std. Deviation
Age	120	28	88	55.2833	14.15828
BMI	120	17	36	25.1833	3.70551
RR	120	17	70	37.425	11.3372
PR	120	58	256	108.4833	31.468
T	120	34.9	42	38.2991	1.56937
SYSBP	120	59	186	109.3583	32.78496
DYABP	120	36	150	76.6	23.28068
MAP	120	43.67	162	87.5194	25.77746

PP	120	9	81	32.7583	15.75121
SPo2	120	51	95	70.5417	10.12352
PaO2	120	45	90	72.8667	8.33534
PaCO2	120	18	118	58.85	17.13008
HCO3	120	8	45	18.265	5.31918
PH	120	6.4	7.8	7.1627	0.24054
H	120	17.28	288	86.8891	45.4878
BE	120	-10	1	-4.7523	2.23362
WBC	120	1950	24000	9203.0833	5454.94515
Lymph	120	204	9250	2195.3858	2205.69205
PLT	120	76000	650000	236312.775	116560.6291
Hb	120	5	17	11.2667	3.007
CRP	120	1	289	62.5	69.04486
LDH	120	60	1969	591.9833	321.83231
ESR	120	20	235	102.8333	51.57035
PCT	120	0.01	6.23	1.1064	1.45226
Na	120	110	180	136.7167	13.09576
K	120	1.9	7.35	4.3675	1.05637
Ca	120	6	17.6	9.9747	2.09112
ALT	120	10	124	42.7417	20.91539
AST	120	12	116	50.8167	24.5976
Glucose	120	67	450	137.5583	62.23145
Cr	120	0.1	11.6	1.0825	1.58283
BUN	120	5	270	27.925	31.77234
SOFA	120	3	9	5.4	1.23941
APACHE	120	10	39	21.15	6.85951
BUN/Cr	120	1.96	260	51.366	45.11775
HCT	120	15	51	33.8	9.02101
SF	120	57.78	260	124.8904	46.73855
PF	120	50	270	128.9093	47.01572
CRPLDH	120	0.19	150	11.5521	16.02828
CRPESR	120	0.81	508.89	76.1334	87.72078
ESRLDH	120	2.63	180	24.2544	25.16076

Table 3: Comorbid Conditions and Outcome The correlation coefficient is Phi=72% and the Cramer correlation coefficient is 52%.

Crosstab					
		Outcome			Total
		Recovery/Discharge within 14 days	Expired within 14 days	Remained in ICU more than 14 days	
Comorbid Conditions	None	19	0	12	31
	Any	2	23	2	27
	ARDS	0	15	8	23
	Acute renal injury	1	7	4	12
	Acute respiratory injury	3	6	3	12
	Septic shock	0	6	4	10
	Ventilator-associated pneumonia	1	2	2	5
Total		26	59	35	120

Table 4: Blood groups and Outcome

		Outcome			Total
		Recovery/Discharge within 14 days	**Expired within 14 days**	**Remained in ICU more than 14 days**	
Blood Groups	A	6	21	9	36
	B	5	15	11	31
	AB	3	16	4	23
	O	12	7	11	30
Total		26	59	35	120

The correlation coefficient is Phi=35% and the Cramer correlation coefficient is 25%.

Table 5: Background disease and Outcome

		Outcome			Total
		Recovery/Discharge within 14 days	**Expired within 14 days**	**Remained in ICU more than 14 days**	
Background Disease	Any	5	2	5	12
	Endocrine system disease	6	9	5	20
	Cardiovascular and cerebrovas-cular diseases	5	18	7	30
	Digestive system disease	0	11	5	16
	Malignant tumor	1	4	2	7
	Nervous system disease	1	3	1	5
	Respiratory system disease	2	9	6	17
	Kidney disease	1	1	0	2
	None	5	2	4	11
Total		26	59	35	120

The correlation coefficient is Phi=41% and the Cramer correlation coefficient is 29%.

Table 6: One-way ANOVA

		Sum of Squares	**Mean Square**	**F**	**Sig.**
WBC	Between Groups	225832991.8	112916495.9	3.985	0.021
	Within Groups	3315181767	28334886.9		
	Total	3541014759			
Lymph	Between Groups	65614510.76	32807255.38	7.478	0.001
	Within Groups	513329702	4387433.35		
	Total	578944212.8			
CRP	Between Groups	43513.684	21756.842	4.86	0.009
	Within Groups	523782.316	4476.772		
	Total	567296			
LDH	Between Groups	2021605.415	1010802.707	11.478	0
	Within Groups	10303942.55	88067.885		
	Total	12325547.97			
ESR	Between Groups	46416.189	23208.095	10.054	0
	Within Groups	270064.478	2308.243		
	Total	316480.667			
PCT	Between Groups	16.271	8.136	4.056	0.02
	Within Groups	234.706	2.006		
	Total	250.977			

T	Between Groups	19.207	9.603	4.103	0.019
	Within Groups	273.882	2.341		
	Total	293.089			
PP	Between Groups	2101.248	1050.624	4.483	0.013
	Within Groups	27422.744	234.382		
	Total	29523.992			
PH	Between Groups	0.617	0.308	5.754	0.004
	Within Groups	6.269	0.054		
	Total	6.886			
SPo2	Between Groups	1363.175	681.587	7.362	0.001
	Within Groups	10832.617	92.586		
	Total	12195.792			
PaO2	Between Groups	1134.907	567.453	9.308	0
	Within Groups	7132.96	60.965		
	Total	8267.867			
PaCO2	Between Groups	2018.609	1009.305	3.589	0.031
	Within Groups	32900.691	281.202		
	Total	34919.3			
H	Between Groups	16485.839	8242.92	4.198	0.017
	Within Groups	229741.812	1963.605		
	Total	246227.651			
CRPLDH	Between Groups	1520.916	760.458	3.063	0.049
	Within Groups	29050.87	248.298		
	Total	30571.785			
CRPESR	Between Groups	96725.399	48362.699	6.909	0.001
	Within Groups	818971.958	6999.76		
	Total	915697.357			
ESRLDH	Between Groups	3982.393	1991.196	3.265	0.042
	Within Groups	71352.228	609.848		
	Total	75334.621			
BUN	Between Groups	9923.339	4961.67	5.268	0.006
	Within Groups	110204.986	941.923		
	Total	120128.325			
SOFA	Between Groups	53.491	26.746	24.2	0
	Within Groups	129.309	1.105		
	Total	182.8			
APACHE	Between Groups	2538.559	1269.28	48.52	0
	Within Groups	3060.741	26.16		
	Total	5599.3			

Tukey post hoc test was used to follow the mean difference of quantitative parameters.

In this study, to compare the mean of the measured parameters before intubation and treatment outcome, one-way variable analysis of variance was used and the results were reported as follows [Table 6]. The results of this test showed that the amount of hydrogen ion in group 1 patients (65.28±28.07) was significantly (95.37±54.96) less than group 3 patients (P-Value=0.013). Regarding the ratios of inflammatory markers, the ratio CRP/LDH% was higher in group 1 patients (16.46±12.75) than group 3 patients

(8.13±7.21) (P-Value=0.049). CRP/ESR% ratio in group 1 patients was significantly higher (P-Value=0.003) than group 2 patients (73.60±21.66) and 3 patients (65.25±19.69). Also, the ESR/LDH% ratio in group 1 patients was significantly lower (P-Value=0.047) than group 3 patients (-15.33±6.39). No significant difference was found in the mean serum creatinine of patients in group 3 (P-Value=0.08). The mean of blood urea nitrogen was significantly lower in group 2 patients (21.28±11.88) than other patients. BUN/Cr ratio was not significantly different in treatment outcome in different groups.

In comparison with the mean of vital signs, body temperature was significantly (P-Value=0.02) in group 1 compared to groups 2 (-1.08±0.39) and 3 (-0.86±0.36). The oxygen saturation (SPO2%) in group 1 patients was significantly (P-Value=0.01) higher than group 2 patients (9.03 ± 2.42) and (P-Value=0.04) in group 3 patients (7.38±2.26). The mean blood pH of patients in group 1 (7.19±0.19) was significantly (P-Value=0.004) higher than patients in group 2 (7.12±0.25) and group 3 (7.12±0.23). The mean absolute amount of hydrogen ion was similarly (P-Value=0.01) higher in patients who died within 14 days (95.37±54.96) than the other two groups. The mean values of relative pressure of carbon dioxide in groups 2 and 3 were significantly higher than those in group 1. The mean serum bicarbonate was higher in group 1 patients than other groups. Mean white blood cell count (P-Value=0.02) in group 2 patients was higher than group 3 patients (2984.74±1135.70).

In addition, total lymphocyte count in group 2 patients was higher than both groups, (P-Value=0.02) and (1875.95±542.31) compared to group 1 and to group 3 (P-Value=0.04) (146.86±446.89). In this regard, the mean absolute lymphocyte count in group 1 patients (1444.14 11 1189.89±1489.14) was significantly lower (P-Value=0.00) than group 3 (1859.23±1968.49) and group 2 (3320.10±2728.84). Mean pulse pressure was significantly different in 3 groups of patients (P-Value=0.01). This value was higher in patients in group 1 (40.50±19.21) than in groups 3 (31.45±14.67) and 2 (29.20±12.96). This difference shows that patients discharged from ICU maintained a more normal range than other groups. The mean SOFA score in group 3 patients (P-Value=0.00) was higher than group 1 patients (1.58±0.24) and 2 patients (1.05±0.22). Consistent with this mean, APCHE score in this group of patients was significantly higher (P-Value=0.00) than the other two groups of patients (9.98±1.20) compared to group 1 and (8.51±1.09) compared to group 2.

Discussion

Numerous cases before intubation can affect the treatment outcome of patients. The underlying disease or comorbid conditions of patients during hospitalization in the intensive care unit can affect the therapeutic outcome of patients. Patients with several comorbid conditions, such as aspiration pneumonia and septic shock, had the highest mortality in 14 days. Patients with Respiratory Distress Syndrome were also ranked second in mortality or hospitalization for more than 14 days. One study state that ARDS is one of the most common comorbid conditions in patients [22]. The results of a meta-analysis show that hypertension, diabetes, cardiovascular disease, and respiratory diseases were the most common conditions in patients [55]. Also, the results of an analysis show that in addition to hypertension and diabetes being the most common condition of patients, 8.2% of patients had more than one condition [56]. Although the highest rate of death occurred among patients with blood type A and the highest rate of ICU discharge was seen in patients with blood type O, it cannot be said that blood type O alone has a protective effect against disease caused by the virus and more research is needed.

One of the most important laboratory parameters studied was WBC, which on average showed mild leukocytosis in patients, as previously found by studies [35,36,38,40]. However, some studies have found leukopenia to be a more common finding in patients. They know [37]. Leukocytosis was evident in patients who remained in the ICU for more than 14 days and no significant differences were found between patients in groups 1 and 3. Lymphopenia was a common finding among patients before intubation that is consistent with the results of previous studies [37-39,41]. Lymphopenia has also been shown to be associated with poor prognosis and can be a measure of disease severity [39]. Lymphopenia, or lymphocytopenia, is a decrease in the number of circulating lymphocytes, often in which the lymphocyte count is less than 2,500 Lymphocytes Per Microliter (LCM). Patients discharged from the ICU experienced more severe lymphopenia than the other groups. The cause of lymphopenia in this group of patients may be due to the use of high doses of corticosteroids, underlying diseases, or malnutrition.

The results of a meta-analysis showed that lymphopenia is directly related to the severity of the disease and less than 1,500 lymphocytes can predict clinical outcome [59]. Patients who remained in the ICU for more than 14 days had the highest mean lymphocyte count [40]. Serial evaluation of lymphocyte count seems to be a predictor of patient outcome [41]. Chronic diseases and aging cause chronic endothelial dysfunction. Endothelial dysfunction causes separation of intercellular junctions, endothelial cell death, and rupture of the blood-tissue barrier with increased adhesion and leukocyte leakage, which may play a role in explaining the lymphopenia observed in severe COVID-19 patients [60]. It can be said that high lymphocyte counts (more than 3320) predict long-term stay of patients in the ICU. No significant platelet count was found, and on average patients' platelets were within the normal range (thrombocytopenia and thrombocytosis were very rare). Studies have shown that thrombocytopenia is associated with disease severity [42-44] and is a common finding in these patients.

Unlike studies [35] that reported PaO2/FiO2 and SPO2/FiO2 ratios in the evaluation and prognosis of acute lung injury and respiratory distress syndrome, in the present study, no significant results (P-Value=0.7) were found between these two ratios with the prognosis of coronavirus pneumonia 2019 [45,46]. Various studies have addressed the importance of inflammatory markers in the diagnosis and severity of coronary heart disease. Procalcitonin is one of the factors that affect the outcome of treatment [47]. However, the diagnostic value of this factor seems to be lower than CRP and interleukin-6 (alone) [48]. One of the factors influencing the therapeutic outcome in this study was lactate dehydrogenase index, which various studies confirm the importance of this inflammatory index in the evaluation and response to treatment of coronavirus-induced pneumonia [49,50], so that increasing this index indicates high disease severity and its reduction indicates an appropriate response to treatment and prognosis of patients [41].

Reactive protein C is one of the inflammatory markers that in the early stages of the disease is widely associated with the severity and spread of the disease [45,46]. However, in this study, no significant association was found with high CRP levels prior to intubation and treatment outcome. Of course, values above 50 of these factors can predict the severity of the disease. Arterial/venous blood gas parameters (PH, PaO2, PaCO2, HCO3, H+) influenced the therapeutic outcome of patients. The mean pH of all patients was less than 7.35. This indicates that all patients had some degree of acidosis before intubation. However, the discharged patients PH ranged from 7 to 7.38 which was near to 7.35. Patients in group 2 ranged from 7.37 to 6.97 and patients in group 3 ranged from 7.35 to 6.99, indicating a higher severity of acidosis in these two groups of patients. The amount of hydrogen ions, which is directly related to blood pH, was similarly higher in group 3 patients than in groups 2 and 1 (respectively) [51-58].

High levels of relative pressure of carbon dioxide in group 2 and 3 patients may indicate acute respiratory failure or respiratory distress syndrome in these patients before intubation. Group 1 patients had normal serum bicarbonate levels before intubation, while the other two groups experienced a decreased mean. This decrease may indicate metabolic disorders such as metabolic acidosis or diabetic ketoacidosis [59-60]. The results of some studies show that patients with coronavirus show some degree of respiratory and metabolic acidosis [4,61]. Since many patients also have diabetes, monitoring bicarbonate levels to prevent diabetic ketoacidosis or ketosis can be helpful. COVID-19 infection appears to cause ketosis or ketoacidosis and induce diabetic ketoacidosis in diabetics, and ketosis can increase mortality and length of hospital stay [62]. Although the mean serum creatinine of patients in all 3 groups was not significantly different, the amount of blood urea nitrogen in patients in group 1 was higher than in groups 2

and 3. This increase may be related to acute renal impairment or sampling/laboratory error or drug side effects.

However, Glomerular Filtration Rate (GFR) was not calculated in patients, so increasing blood urea nitrogen alone in group 1 patients alone could not indicate acute renal impairment. However, mean blood urea nitrogen was lower in patients who were in the ICU for more than two weeks than in other patients. BUN/Cr ratio, considering that this ratio is a good indicator for differentiating the causes of pre-renal or post-renal failure, and the mean increase (51.36±45.11) in all patients, can be said to be one of the reasons for increasing this value which can be caused by causes such as gastrointestinal bleeding [53], decreased renal perfusion, shock, hypovolemia, hypotension and dehydration. Serum Nitrogen Urea (BUN), Creatinine (Cr), Urinary Inhibitor C (CysC) and Retinol-Binding Protein (RBP) can be used for early detection of kidney damage [54]. SOFA and APACHE scores were significantly associated with treatment outcome in all three groups of patients. These two criteria were higher in patients who died within 14 days than in the other two groups. Also, patients who were hospitalized in the intensive care unit for more than 14 days had higher scores than patients who were discharged from the intensive care unit for 14 days.

In this study, SOFA and APACHE scores were measured only once before intubation. Since the frequency of SOFA score is more important, it is recommended to calculate the SOFA score serially for patient follow-up.

Pulse pressure is the difference between systolic and diastolic blood pressure [57] and is one of the parameters that had a significant impact on the outcome of treatment. Normal values are 40 mm Hg, in the presence of hypoperfusion, flattening of the pulse pressure is due to Systemic Vascular Resistance (SVR). Low blood pressure can also be a sign of heart problems despite a narrow pulse pressure. Patients discharged from the ICU maintained a normal mean, while patients who died had a lower mean and patients who remained in the ICU had a lower mean. The most common cause of low pulse pressure is a drop in left ventricular shock volume. In trauma, low or narrow pulse pressure indicates significant blood loss [58] (insufficient preload leads to decreased cardiac output).

Due to the significant decrease in pulse pressure in both groups of patients, it seems that these patients have some degree of heart failure, shock, aortic stenosis or in some cases cardiac tamponade. In this study, by examining different criteria, we obtained three inflammatory ratios that can be helpful in determining the prognosis of patients who have an indication for intubation. CRP/ESR%, ESR/LDH% and CRP/LDH% ratios had a significant effect (respectively) in determining the prognosis of patients. Due to the small number of quantitative values, the percentage of these parameters was

used. The CRP/LDH% ratio was lower in patients who died than in other groups, and discharged patients had the highest mean. CRP/ESR% ratio was higher in discharged patients than other groups and had the lowest mean in group 2. However, ESR/LDH% had the highest mean in group 2 and the lowest mean in group 1.

As in a study based on blood group association and coronavirus infection and therapeutic outcomes, a significant association was found in this study, indicating higher mortality in people with blood type A than in other blood groups. Also, the lowest death rate was observed among people with blood type O. Although some studies suggest [61] BCG vaccination can have a positive effect on the immune system against Covid-19, but in this study, no relationship was found between vaccination and therapeutic outcome and even the severity of the disease [62]. Limitations of this study include the extent of patients in the intensive care units of Imam Khomeini Hospital. Also, due to the critical situation, there may be errors in data collection, laboratory reports and even blood sampling.

Conclusion

According to the results, white blood cell count and absolute lymphocyte count, blood urea nitrogen, SOFA and APACHE scores, CRP/LDH%, CRP/ESR% and ESR/LDH% Arterial blood gas indices, pulse rate and patient temperature before intubation are among the parameters that can affect the patient's 14-day prognosis. The CRP/LDH% ratio seems to be a good indicator for predicting the prognosis of discharge or death of patients within 14 days, but CRP/ESR% and ESR/LDH% are suitable criteria for determining the prognosis of discharge or stay of more than 14 days in Be ICU. Inflammatory ratios were obtained experimentally from this study, and the reliability and cut-off determination of these values require further research. Mortality seems to be higher among people with blood type A than other blood groups. No significant relationship has been found between BCG vaccination and therapeutic outcome of patients.

The patient's comorbid conditions had a significant effect on treatment outcome, although the underlying disease did not differ significantly in treatment outcome. However, further studies are needed to investigate the effect of underlying disease on treatment outcome or mortality in patients. We would like to thank all the esteemed staff of Imam Khomeini Hospital in Tehran. Special thanks to the doctors, nurses and all the clinical staff of the intensive care unit who helped us in this project in times of crisis. The researchers have been greatly thanked and appreciated.

Funding

Acknowledgments

Conflicts of Interest

The authors declare no conflict of interest.

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